Attorney Docket No. TMT-10902/04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF APPEALS AND INTERFERENCES

Applicant: Michael T. Trese et al.

Serial No.: 10/068,314 Group Art Unit: 3763

Filed: February 6, 2002 Examiner: Matthew F. DeSanto

For: METHOD FOR VITREOUS LIQUEFACTION

BRIEF ON APPEAL

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I. Real Party in Interest.

The real party in interest in this appeal is the assignee, NuVue Technologies, Inc.

II. Related Appeals and Interferences.

Appellant is aware of no appeals or interferences pending or otherwise related to the present appeal.

III. Status of the Claims.

All of the pending claims (1-10, 13-21, 24-28) stand finally rejected.

No claims are allowed.

All of the pending claims, claims 1-10, 13-21 and 24-28, are appealed claims.

IV. Status of the Amendments.

A. Amendment to the Claims

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1. (Previously Presented) A process for human vitreous liquefaction comprising the steps of:

delivering a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a subject human eye; and

incubating the plasmin in the vitreous body for a predetermined amount of time to create a liquefied vitreous.

2. (Original) The process of claim 1 wherein the delivering is by injection.

3. (Original) The process of claim 1 wherein the delivering is by infusion.

4. (Original) The process of claim 1 wherein the delivering is by sustained release intraocular device.

5. (Previously Presented) The process of claim 1 wherein the plasmin comprises human plasmin.

6. (Previously Presented) The process of claim 1 wherein the plasmin comprises autologous human plasmin.

7. (Previously Presented) The process of claim 1 wherein the plasmin comprises an accompaniment selected from the group consisting of: an enzyme, a glycoprotein, a

polysaccharide, an antibiotic, a pharmaceutically acceptable diluent, a pharmaceutically acceptable adjuvant and a pharmaceutically acceptable carrier.

8. (Original) The process of claim 1 further comprising the step of delivering a plasmin inhibitor.

9. (Original) The process of claim 1 wherein the subject eye has a pathological condition.

10. (Original) The process of claim 9 wherein the pathological condition is selected from the group consisting of: diabetic retinopathy, macular hole, macular pucker, intraocular infection, foreign intraocular material and retinal detachment.

Claims 11 and 12 (Canceled)

13. (Currently Amended) The process of claim 1 wherein the predetermined amount of time is between ten minutes and two hours.

14. (Previously Presented) A process for human vitreous liquefaction comprising the steps of:

delivering a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters comprising autologous plasmin into a vitreous body of a subject human eye; and

incubating the plasmin in the vitreous body for a predetermined amount of time to induce vitreous liquefaction.

15. (Original) The process of claim 14 wherein the delivering is by injection.

16. (Original) The process of claim 14 wherein the delivering is by infusion.

17. (Original) The process of claim 14 wherein the delivering is by sustained release intraocular device.

18. (Previously Presented) The process of claim 14 wherein the plasmin comprises an accompaniment selected from the group consisting of: an enzyme, a glycoprotein, a polysaccharide, an antibiotic, a pharmaceutically acceptable diluent, a pharmaceutically acceptable adjuvant and a pharmaceutically acceptable carrier.

19. (Original) The process of claim 14 further comprising the step of delivering a plasmin inhibitor.

20. (Original) The process of claim 14 wherein the subject eye has a pathological condition.

21. (Original) The process of claim 20 wherein the pathological condition is selected from the group consisting of: diabetic retinopathy, macular hole, macular pucker, intraocular infection, foreign intraocular material and retinal detachment.

Claims 22 and 23 (Canceled)

24. (Previously Presented) The process of claim 14 wherein the predetermined amount of time is between ten minutes and two hours.

25. (Previously Presented) The process of claim 1 further comprising the step of suctioning the liquefied vitreous from the subject human eye.

26. (Previously Presented) The process of claim 25 wherein suctioning is performed through a 25 or finer gauge instrument.

27. (Previously Presented) The process of claim 14 further comprising the step of suctioning the liquefied vitreous from the subject human eye.

28. (Previously Presented) The process of claim 27 wherein suctioning is performed through a 25 or finer gauge instrument.

V. Summary of the Claimed Subject Matter.

The present invention of independent claim 1 relates to a process for vitreous liquefaction (page 3, lines 1-2) comprising delivery of plasmin into the vitreous body of an eye (page 3, line 23 – page 4, line 1) and incubating the plasmin in the vitreous for a predetermined amount of time to cause liquefaction (page 4, line 2). Independent claim 14 recites delivery of an autologous plasmin into the vitreous of an eye (page 6, line 5) and incubating the autologous plasmin in the vitreous body for a predetermined amount of time to cause liquefaction (page 5, line 14 – page 6, line 2).

VI. Grounds of Rejection to Be Reviewed on Appeal.

Pending claims 1-7, 9, 10, 13-18, 20 and 21 stand rejected under 35 U.S.C. §102(b) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) over Trese et al. (Ophthalmology, Vol. 105, Issue 9, 1 September 1998, pp. 1617-1620), hereinafter referred to as Trese et al. (Ophthalmolgy). Pending claims 8, 19 and 25-28 stand rejected under 35 U.S.C. §103(a) over Trese et al. as detailed above further in view of Trese et al. (American Academy of Ophthalmology, ISSN 1607-1610), hereinafter referred to as Trese et al. (American). Although the Examiner did not specifically state in the Office Action Summary dated March 24, 2005 (page 2, item # 3) that claim 24 is rejected, the Applicant assumes that claim 24, being similar in scope to claim 13, stands rejected under 35 U.S.C. §102(b) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) over Trese et al. (Ophthalmology). Thus, claims 1-7, 9, 10, 13-18, 20, 21 and 24 stand rejected as being anticipated or in the alternative obvious over Trese et al. (Ophthalmology), while claims 8, 19 and 25-28 stand rejected as being obvious over Trese et al. (Ophthalmology) in view of Trese et al. (American). Appellant will present arguments directed solely to these two issues.

VII. Argument.

A. The Examiner's Position.

The Examiner has based the rejection of claims 1-7, 9, 10, 13-18, 20, 21 and 24 under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Trese et al. (Ophthalmology). Trese et al. (Ophthalmology) is cited for teaching the delivery of autologous human plasmin into a vitreous body of an eye and then incubating the eye. Trese et al. (Ophthalmology) is further cited for teaching the use of a dose of 0.4 IU of plasmin. The Examiner in an Office communication dated March 24, 2005 states:

> At the time of the invention it would have been obvious for one of ordinary skill in the art to modify the teachings of Trese et al. because it is well known in the medical field art to vary the dose size that would be injected into a patient, since medication usually depends on the size of the patient as well as the area in which the injection will occur. This concept is well known in the research art and can be seen in the previous cited prior art.

The Examiner has based the rejection of claims 8, 19 and 25-28 under 35 U.S.C. §103(a) as being unpatentable over Trese et al. (Ophthalmology) as applied to the claims, and further in view of Trese et al. (American). The Examiner believes motivation to combine the references is found in the skill of one of ordinary skill in the art:

> Trese et al. (Ophthalmology) discloses the claimed invention but fails to specifically point out the use of a plasmin inhibitor and the actual size of the needle being used to remove the liquefaction that occurred in the eye.
>
> Trese et al. (American) discloses the use of a plasmin for the liquefaction of the eye as well as the use of small gauge needles for sucking material out of the eye and the use of a plasmin inhibitor to reduce to the activity of the plasmin that was injected into the eye.
>
> At the time of the invention it would have been obvious for one of ordinary skill in the art to combine the teachings of Trese et al.

(Ophthalmology) with Trese et al. (American) because Trese et al. (American) provides further explanation as to why those steps are necessary. Trese et al. (American) also discloses the level of skill in the medical art since it is well known in the art to perform these steps.

B. Appellant's Position as to Patentability of All Depending Claims.

1. Appellant's Position as to the Patentability of Claims 1-7, 9, 10, 13-18, 20, 21 and 24 as Being Rejected Under 35 U.S.C. §102(b) as Anticipated by Trese et al. (Ophthalmology).

The teaching of Trese et al. (Ophthalmology) is limited to a process for macular hole treatment and thus clearly fails to anticipate the present invention. It is a tenet of patent law that anticipation has always been held to require absolute identity and process between the claimed process and a process disclosed in a single reference. In *Richardson v. Suzuki Motor Co., Ltd.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) it was stated, "Every element of the claimed invention must be literally present, arranged as in the claim."

Independent claim 1 recites delivering a dose of plasmin of less than 0.4 units and "incubating the plasmin in the vitreous body [of a subject human eye] for a predetermined amount of time to create a liquefied vitreous." Independent claim 14 limits the present invention to the use of autologous plasmin. Thus, the present invention as a process is indicated when it is necessary to liquefy the vitreous from the eye and not merely to detach the congealed vitreous adhered to the retina. As the instant specification makes clear at page 1, line 8 – page 2, line 3, the application of mechanical forces to remove adhered vitreous is associated with a number of complications involved in vitrectomy. The inventive process of independent claim 1 and independent claim 14 is indicated to reduce the vitreous viscosity to a liquid state in advance of, or potentially to preclude vitrectomy.

In contrast to the invention of claim 1 and claim 14, Trese et al. (Ophthalmology) teaches a process for macular hole treatment in pediatric patients. A macular hole is a small break in the macula located in the center of the eye's light sensitive retinal tissue. The macula provides for the sharp central vision associated with reading, driving and discerning fine detail. As such, the macular hole is associated with blurred and distorted central vision. As noted in Trese et al. (Ophthalmology) at the second paragraph under the discussion section, plasmin enzyme is known to loosen or actually separate the vitreoretinal junction. The paragraph concludes with "plasmin enzyme facilitated surgical cleavage of the vitreoretinal interface."

As Trese et al. (Ophthalmology) teaches loosening or separation of the vitreoretinal junction but fails to teach the recited claim element of actually liquefying the vitreous, Appellant submits that Trese et al. (Ophthalmology) fails to anticipate the claimed invention. Therefore, it is believed that independent claim 1, independent claim 14 and those that depend therefrom are patentable over Trese et al. (Ophthalmology).

2. Appellant's Position as to the Rejection of Claims 1-7, 9, 10, 13-18, 20, 21 and 24 Under 35 U.S.C. §103(a) as Obvious Over Trese et al. (Ophthalmology).

Appellant hereby incorporates by reference the above remarks with respect to independent claim 1, independent claim 14 and Trese et al. (Ophthalmology).

Using hindsight reconstruction, the Examiner has concluded that the present invention is obvious over Trese et al. (Ophthalmology). However, an Examiner may not, because of doubt that the invention is patentable, resort to speculation, unfounded assumption or hindsight reconstruction to supply deficiencies in the factual basis for the rejection. See *In re Warner*, 379 F.2d 1011, 1017, 154 USPQ 173, 177 (CCPA 1967), *cert. denied*, 389 U.S. 1057 (1968). Rather, in determining obviousness, "the [E]xaminer can satisfy the burden of showing obviousness of

the combination 'only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.'" *In re Lee*, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002), citing *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). "Mere denials and conclusory statements, however, are not sufficient to establish a genuine issue of material fact." *Dembiczak*, 175 F.3d at 999-1000, 50 USPQ2d at 1617, citing *McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed. Cir. 1993).

Appellant submits that the claimed invention is nonobvious over Trese et al. (Ophthalmology) since the separation of the vitreous from the dissimilar retinal tissue is a less effective vitreal treatment, as compared to the claimed invention. The liquefaction of the vitreous represents not only a separation but a dissolution of the gelled vitreous. As there is neither a teaching nor contemplation that plasmin injected into a subject eye according to Trese et al. (Ophthalmology) is able to induce vitreous liquefaction, it is submitted that this higher level of performance as recited in claim 1 and claim 14 is not obvious in light of Trese et al. (Ophthalmology).

The notion that one skilled in the art would be motivated to deliver a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a subject human eye and incubate the plasmin for a predetermined amount of time *to create a liquefied vitreous* is not provided by the prior art of Trese et al. (Ophthalmology). Appellant submits that the only motivation for the above described process is found in the pending application and hindsight reconstruction is improper. Therefore, it is believed that independent claim 1,

independent claim 14 and those that depend therefrom are patentable over Trese et al. (Ophthalmology).

3. Appellant's Position as to the Rejection of Claims 8, 19 and 25-28 Under 35 U.S.C. §103(a) as Obvious Over Trese et al. (Ophthalmology) and Further in View of Trese et al. (American).

Appellant submits that these claims are allowable on the basis of dependency from an allowable base claim and incorporates by reference the above remarks with regard to Trese et al. (Ophthalmology). Appellant further submits that the prior art reference combination fails to yield the claimed invention of claims 8, 19 and 25-28 not only for the reasons cited above but also based on the fact that Trese et al. (Ophthalmology) and further in view of Trese et al. (American) fails to provide a teaching or motivation for vitreous liquefaction and instead only would indicate to one of skill in the art that vitreoretinal separation is possible.

In *In re Wesslau* (1965), the Court of Customs and Patent Appeals cautioned that "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). The Federal Circuit has held that a single line in a prior art reference taken out of context and relied upon with the benefit of hindsight is impermissible to show obviousness. Instead, a reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448, 230 USPQ 416, 419-420 (Fed. Cir. 1986), *cert denied*, 484 U.S. 823 (1987). Also, the Federal Circuit noted "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or

would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Trese et al. (American) is submitted to be deficient in lacking a teaching or motivation for the creation of a liquefied vitreous. Rather, Trese et al. (American), like Trese et al. (Ophthalmology), pertains to macular holes and only teaches the creation of a traumatic posterior vitreous separation. While both references admittedly teach the creation of a vitreoretinal separation, also detailed as a posterior vitreous detachment (PVD), both references alone or in combination fail to contemplate or teach a higher level of effect, namely vitreous liquefaction as compared to vitreoretinal separation.

In addition, Trese et al. (American) teaches away from the present invention. In the discussion section of Trese et al. (American) it states:

> The dose of 0.4 IU of autologous plasmin enzyme, which seems optimal for producing a PVD in humans, does not show the *reliable* liquefaction of vitreous that was seen in animals. This suggests to us that a vitreous cutter is still necessary to safely remove the partially liquefied vitreous, making space for gas used in the postoperative management of stage 3 macular holes. We believe that this study demonstrates that it is possible to achieve spontaneous posterior vitreous separation and closure of macular holes in the human eye but that liquefaction of the vitreous gel is *variable* in human eyes at the dose of 0.4 IU. (emphasis added)

Based on these comments in the prior art, Appellant submits that one "of ordinary skill [in the art], upon reading [this] reference, ... would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*. In other words, at the time of the invention one of ordinary skill in the art would have modified the teachings of Trese et al. (Ophthalmology) and Trese et al. (American) by varying the dose to *greater* than 0.4 IU of autologous plasmin for reliable liquefaction of the vitreous in humans, *not less than* 0.4 IU.

It is also of interest to note that one with apparent ordinary skill in the art did in fact comment on the "six potential goals" of the "use of plasmin intravitreally during macular hole surgery" (see Discussion by Jay S. Duker, M.D. included within Trese et al. (American)). These six potential goals outlined by one skilled in the art were: 1) reducing the suction levels and therefore the traction on the retina when surgically inducing a PVD; 2) minimizing the need for delicate and difficult dissection of the internal limiting membrane; 3) decreasing operating time; 4) improving visual outcome; 5) decreasing complications; and 6) possibly enabling macular hole surgery to become an office-based procedure. The reduced "suction levels" mentioned above in goal #1 was discussed in the context of the plasmin being used because of "its activity on laminin and fibronectin, two molecules responsible to a large degree for the adhesion between the anterior retina and the posterior hyaloid." Nowhere is it mentioned that the use of less than 0.4 IU of plasmin could have a potential for liquefaction of a human vitreous. In other words, it was not obvious to this individual skilled in the art to combine the teaching of Trese et al. (Ophthalmology) and Trese et al. (American) to deliver a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a human eye and incubate the plasmin in the vitreous body for a predetermined amount of time *to create a liquefied vitreous*.

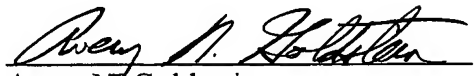
On the basis of the above remarks Applicant submits that the notion that one skilled in the art would be motivated to deliver a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a human eye and incubate the plasmin in the vitreous body for a predetermined amount of time to create a liquefied vitreous is not provided by the prior art of Trese et al. (Ophthalmology) and further in view of Trese et al. (American). Appellant submits that the only motivation to perform the process disclosed in the present invention is found in the pending application and hindsight reconstruction is improper.

Therefore, it is believed that claims 8, 19 and 25-28 are patentable over Trese et al. (Ophthalmology) and further in view of Trese et al. (American).

VIII. Conclusion.

In summary, the Examiner's references and combination of references that make up the outstanding rejections include a reference that does not anticipate nor make obvious the claims 1-7, 9, 10, 13-18, 20, 21 and 24. Furthermore, the reference Trese et al. (American) teaches away from the present invention and a motivation to deliver a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a human eye and incubate the plasmin in the vitreous body for a predetermined amount of time to create liquefied vitreous is absent, except for within the present application. Accordingly, the anticipation rejection under 35 U.S.C. §102(b) and the obviousness rejection under 35 U.S.C. §103(a) with regard to claims 1-7, 9, 10, 13-18, 20, 21 and 24 should be reversed. Also, the obviousness rejection under 35 U.S.C. §103(a) with regard to claims 8, 19 and 25-28 should likewise be reversed.

Respectfully submitted,



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Janice R. Kuehn

Janice R. Kuehn

APPENDIX A

CLAIMS ON APPEAL

1. A process for human vitreous liquefaction comprising the steps of:

delivering a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters into a vitreous body of a subject human eye; and

incubating the plasmin in the vitreous body for a predetermined amount of time to create a liquefied vitreous.

2. The process of claim 1 wherein the delivering is by injection.

3. The process of claim 1 wherein the delivering is by infusion.

4. The process of claim 1 wherein the delivering is by sustained release intraocular device.

5. The process of claim 1 wherein the plasmin comprises human plasmin.

6. The process of claim 1 wherein the plasmin comprises autologous human plasmin.

7. The process of claim 1 wherein the plasmin comprises an accompaniment selected from the group consisting of: an enzyme, a glycoprotein, a polysaccharide, an

antibiotic, a pharmaceutically acceptable diluent, a pharmaceutically acceptable adjuvant and a pharmaceutically acceptable carrier.

8. The process of claim 1 further comprising the step of delivering a plasmin inhibitor.

9. The process of claim 1 wherein the subject eye has a pathological condition.

10. The process of claim 9 wherein the pathological condition is selected from the group consisting of: diabetic retinopathy, macular hole, macular pucker, intraocular infection, foreign intraocular material and retinal detachment.

13. The process of claim 1 wherein the predetermined amount of time is between ten minutes and two hours.

14. A process for human vitreous liquefaction comprising the steps of:

delivering a dose of plasmin of less than 0.4 units in a volume of about 0.1 cubic centimeters comprising autologous plasmin into a vitreous body of a subject human eye; and

incubating the plasmin in the vitreous body for a predetermined amount of time to induce vitreous liquefaction.

15. The process of claim 14 wherein the delivering is by injection.

16. The process of claim 14 wherein the delivering is by infusion.

17. The process of claim 14 wherein the delivering is by sustained release intraocular device.

18. The process of claim 14 wherein the plasmin comprises an accompaniment selected from the group consisting of: an enzyme, a glycoprotein, a polysaccharide, an antibiotic, a pharmaceutically acceptable diluent, a pharmaceutically acceptable adjuvant and a pharmaceutically acceptable carrier.

19. The process of claim 14 further comprising the step of delivering a plasmin inhibitor.

20. The process of claim 14 wherein the subject eye has a pathological condition.

21. The process of claim 20 wherein the pathological condition is selected from the group consisting of: diabetic retinopathy, macular hole, macular pucker, intraocular infection, foreign intraocular material and retinal detachment.

24. The process of claim 14 wherein the predetermined amount of time is between ten minutes and two hours.

25. The process of claim 1 further comprising the step of suctioning the liquefied vitreous from the subject human eye.

26. The process of claim 25 wherein suctioning is performed through a 25 or finer gauge instrument.

27. The process of claim 14 further comprising the step of suctioning the liquefied vitreous from the subject human eye.

28. The process of claim 27 wherein suctioning is performed through a 25 or finer gauge instrument.

APPENDIX B

EVIDENCE

There is no evidence that has been entered or relied upon in this appeal.

APPENDIX C

RELATED PROCEEDINGS

There are no decisions that have been rendered by a court or the Board in any proceeding identified in the related appeal.